

Product Data Sheet

Product Name: PD-1-IN-1 (CA-170)

Cat. No.: GC19225

Chemical Properties

Cas. No. 1673534-76-3

SMILES C[C@@H](O)[C@@H](C(O)=O)NC(N[C@H](C1=NC([C@@H](N)CO)=NO1)CC(N)=O)=O

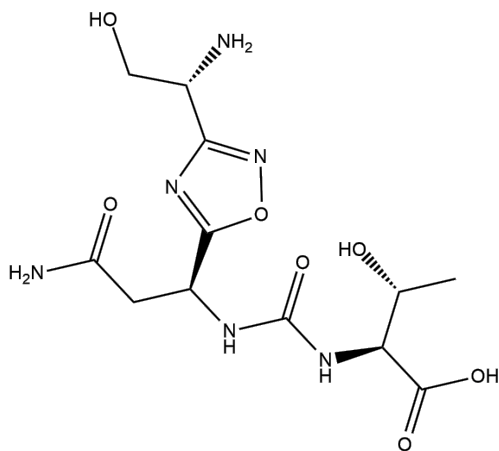
Formula $C_{12}H_{20}N_6O_7$ M.Wt 360.32

Solubility DMSO : 28.5 mg/mL (79.10 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines Human PBMCs

Caution: Product has not been fully validated for medical applications. For research use only.

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Preparation method	Human PBMCs from healthy donors were pre-cultured at high density (1×10^7 cells/ml) for 48 h to increase cell–cell contacts and immune scanning. The cells were then harvested and treated with anti-CD3 or anti-CD3 + anti-CD28 antibodies as positive controls, and PD-1-IN-1 (CA-170) (10 nM to 1000 nM). Release of IL-2, IFN- γ , and TNF- α was measured in the culture supernatants at 48 h.
Reaction Conditions	10-1000 nM ; 48 h
Applications	In human PBMCs, CA-170 did not induce significant IL-2, IFN- γ , and TNF- α levels in both normal culture conditions or high-density culture conditions, while an antibody against CD28 induced as expected.
Animal experiment [2]:	
Animal models	Female A/J mice
Preparation method	Mice were divided into five groups: (a) control mice that received PBS; (b) adjuvant control mice that received a STING agonist plus AddaVax; (c) KVax mice treated with KVax plus adjuvant; (d) PD-1-IN-1 (CA-170) treatment (10 mg/kg in PBS,) by oral gavage five times per week; (e) combined treatment with KVax/adjuvant plus PD-1-IN-1 (CA-170). Mice were administered one dose of the carcinogen vinyl carbamate ³¹ (VC) by i.p. injection (16 mg/kg in sterile saline). PD-1-IN-1 (CA-170) treatment was started one week after VC induction of lung adenocarcinoma.

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Dosage form 10 mg/kg; p.o.

Applications PD-1-IN-1 (CA-170) treatment decreased tumor load by 63% relative to the adjuvant control group.

References:

- [1] Sasikumar P G, Sudarshan N S, Adurthi S, et al. PD-1 derived CA-170 is an oral immune checkpoint inhibitor that exhibits preclinical anti-tumor efficacy[J]. Communications biology, 2021, 4(1): 699.
- [2] Pan J, Chen Y, Zhang Q, et al. Inhibition of lung tumorigenesis by a small molecule CA170 targeting the immune checkpoint protein VISTA[J]. Communications biology, 2021, 4(1): 906.

Background

PD-1-IN-1 (CA-170) is an orally active dual inhibitor of the immune checkpoint regulatory proteins VISTA and PD-L1^[1]. PD-1-IN-1 (CA-170) does not directly bind to the target proteins; its mechanism of action might involve blocking their downstream signaling pathways^[2]. PD-1-IN-1 (CA-170) exhibits anti-tumor activity similar to that of PD-1 monoclonal antibodies and offers advantages in terms of biosafety^[3].

In vitro, PD-1-IN-1 (CA-170) (10-1000nM) treatment of human peripheral blood mononuclear cells (PBMCs) for 48h did not induce the secretion of cytokines IL-2, IFN- γ , and TNF- α , while anti-CD28 antibodies could induce this secretion ^[4].

In vivo, oral administration of PD-1-IN-1 (CA-170) (10 mg/kg) for 14 days inhibited tumor growth in a mouse model of colon cancer by 36%. However, it did not show significant efficacy in severely immunocompromised mice, demonstrating that the efficacy of PD-1-IN-1 (CA-170) relies on an immune-mediated mechanism^[4]. In a mouse model of lung cancer, oral administration of PD-1-IN-1 (CA-170) (10 mg/kg) for 28 days reduced tumor burden by 63%, increased the number of intratumoral CD8⁺ T cells, and inhibited lung cancer metastasis^[5].

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References:

- [1] Lazorchak A S, Patterson T, Ding Y, et al. Abstract A36: CA-170, an oral small molecule PD-L1 and VISTA immune checkpoint antagonist, promotes T cell immune activation and inhibits tumor growth in pre-clinical models of cancer[J]. Cancer Immunology Research, 2017, 5: A36-A36.
- [2] Musielak B, Kocik J, Skalniak L, et al. CA-170—a potent small-molecule PD-L1 inhibitor or not?[J]. Molecules, 2019, 24(15): 2804.
- [3] Wu Q, Jiang L, Li S, et al. Small molecule inhibitors targeting the PD-1/PD-L1 signaling pathway[J]. Acta Pharmacologica Sinica, 2021, 42(1): 1-9.
- [4] Sasikumar P G, Sudarshan N S, Adurthi S, et al. PD-1 derived CA-170 is an oral immune checkpoint inhibitor that exhibits preclinical anti-tumor efficacy[J]. Communications biology, 2021, 4(1): 699.
- [5] Pan J, Chen Y, Zhang Q, et al. Inhibition of lung tumorigenesis by a small molecule CA170 targeting the immune checkpoint protein VISTA[J]. Communications biology, 2021, 4(1): 906.

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